Notice of Allowability	Application No.	Applicant(s)	
	10/003,481	VELLINGER ET AL.	
	Examiner	Art Unit	
	William H. Beisner	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Applicants' communcation dated 10/10/06 and interview dated 10/23/06*.

2. ☒ The allowed claim(s) is/are *5,6,10,18,11,13,15-17,19-22,24,37,26 and 28-36 renumbered as claims 1-26 respectively*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *20061023* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with David W. Carrithers on 10/23/2006.

The application has been amended as follows:

1. (Canceled)

2. (Canceled)

3. (Canceled)

4. (Canceled)

5. (Currently amended) A bioreactor apparatus and cell culturing system providing means for cell sampling, dilution, and fixation, comprising:

a sealed housing enclosing a cell growth reactor vessel;

said [[a]] cell growth reactor vessel rotatable about its axis including a cylindrical side wall connecting a first reactor cover plate and a second reactor cover plate, a first fluid rotary union in said first reactor cover plate providing an inlet for fluid communication with a fluid medium source, a second fluid rotary union in said second reactor cover plate including at least one exit outlet for medium and cells and at least one exit outlet [[is]] in fluid communication with a filter for retaining cells and passage of medium;

means for rotating said reactor vessel about its axis;

means for collecting fluid and cell samples comprising a rotary sample collector including a first stationary collector plate and a second rotatable collector plate in sealed

connection at their centers and in fluid communication with said ~~reactor vessel~~ exit outlet for medium and cells;

said rotary sample collector comprising multiple sample collectors in said ~~second rotatable~~ first stationary collector plate ~~including an inlet rotatably~~ which are alignable with an ~~outlet~~ inlet in said ~~first stationary~~ second rotatable collector plate with capability for collecting cells on filters, fixing the cells and collecting the cells;

means for delivering medium and circulating medium to and from said reactor vessel;

means for controlling the humidity within said sealed housing;

means for rotating said second rotatable collector plate;

a computer with graphical user interface for automatically and/or robotically controlling rotation of the reactor vessel, rotation of ~~said first plate with respect to~~ said second plate, controlling the feeding of fresh medium, controlling perfusing the reactor vessel, controlling taking timed collection samples of fluid from said reactor vessel, and selecting between collecting cells or cell-free supernatant; and

an electrical power source in electrical communication with said means for rotating said reactor vessel, said [[mens]] means for rotating said second collector plate, and said means for delivering and circulating medium.

6. (Currently amended) The bioreactor apparatus and cell culturing system of claim 5 said ~~rotary sample collector including a rotating inlet into~~ first stationary collector plate including a compartment with a filter [[,]] means to remove waste liquid from an input cell suspension,

means for collecting cells in chambers in liquid suspension, and means to store fixed cells for later recovery and examination.

7. (Canceled)

8. (Canceled)

9. (Previously presented) The bioreactor apparatus and cell culturing system of claim 5 further including means for exchanging gases between said cells in said medium and ambient gases comprising a selected length of gas permeable tubing in fluid communication with said cells in said medium and said ambient gas.

10. (Previously presented) The bioreactor and cell culturing system of claim 5 wherein said filter comprises a low pressure drop filter for preventing cells from exiting the reactor when fluid is withdrawn.

11. (Currently amended) The bioreactor apparatus and cell culturing system of claim 5 further including a polymeric fresh-medium storage bag in fluid communication with a peristaltic pump for batch feeding, perfusion or sample collection connecting to said inlet of said reactor vessel through a conduit.

12. (Canceled)

13. (Currently amended) The bioreactor apparatus and cell culturing system of claim 5 wherein said means for controlling the humidity comprises a humidity control system consisting of a polymeric porous matrix and a fan [[;]] .

14. (Canceled)

15. (Previously presented) The bioreactor apparatus and cell culturing system of claim 5 including means for oxygenation of said medium in said reactor.

16. (Previously presented) The bioreactor apparatus and cell culturing system of claim 5 further including analytical sensors for measuring the pH, glucose, and oxygen of said medium.

17. (Previously presented) The bioreactor apparatus and cell culturing system of claim 5 said means for rotating said second rotatable collector plate comprises a stepping motor for rotating and aligning said second rotatable collector plate with said first stationary collector plate.

18. (Previously presented) The bioreactor apparatus and cell culturing system of claim 10, wherein said low pressure drop filter is a polymeric filter.

19. (Previously presented) The bioreactor apparatus and cell culturing system of claim 5, said means for delivering medium and circulating medium to and from said reactor vessel comprises at least one perfusion pump.

20. (Currently amended) The bioreactor apparatus and cell culturing system of claim 5, further comprising:

a camera and an observation system, comprising:

a video frame grabber;

a beam splitter for dual optical view of contents of said rotating cell growth reactor and of cell samples extracted from said cell growth reactor or a microscopic observation slide disposed in a fluid line from said reactor vessel;

at least one LED and a diffuser for providing backlighting for said microscopic observation slide;

at least one LED providing front lighting or oblique lighting for viewing the contents of said cell growth reactor;

a camera attached to said video frame grabber ~~housing containing a~~ and said beam splitter ~~beamsplitter cube~~ wherein a first side of said beam splitter ~~beamsplitter~~ attached to an objective lens for viewing said reactor contents and a second side of said beam splitter ~~beamsplitter~~ attached to a spacer barrel which is attached to said microscopic observation slide.

21. (Currently amended) The bioreactor apparatus and cell culturing system of claim 20, wherein said camera system comprises a color camera and a dual optical path configuration

allowing for a first observation of the rotating cell growth reactor contents with a 20 x 25mm Field Of View (FOV) and a second microscopic observation path providing an approximately 5-micron resolution of cell samples that have been extracted from the reactor vessel ~~bioreactor~~ and pumped into the observation slide [[cell]].

22. (Previously presented) The bioreactor apparatus of claim 21, wherein said camera in said camera system is a digital camera and/or a video device for showing instantaneous or still frame pictures.

23. (Canceled)

24. (Currently amended) The bioreactor apparatus of claim 20 further comprising a turning prism in optical communication with said cell growth reactor vessel and a foil type heater in radiant communication with said turning prism to prevent condensation.

25. (Canceled)

26. (Currently amended) A closed-loop bioreactor apparatus and cell culturing system, comprising:

~~a reactor vessel;~~

a cell growth reactor vessel rotatable about its axis including a cylindrical side wall connecting a first reactor cover plate and a second reactor cover plate, a first fluid rotary union in

said first reactor cover plate providing an inlet for fluid communication with a fluid medium source, a second fluid rotary union in said second reactor cover plate including at least one exit outlet for medium and cells and at least one exit outlet [[is]] in fluid communication with a filter for retaining cells and passage of medium;

~~an electrical power source in electrical communication with said means for rotating said reactor vessel, said mens for rotating said second collector plate, and said means for delivering and circulating medium;~~

means for rotating said reactor vessel about its axis;

means for collecting fluid and cell samples comprising a rotary sample collector including a first stationary collector plate and a second rotatable collector plate in sealed connection at their centers and in fluid communication with said ~~reactor vessel~~ exit outlet for medium and cells;

said rotary sample collector further comprises means for rotating an inlet in second rotatable collector plate into a compartment in said first stationary collector plate with filter [[,]] means to remove waste liquid from an input cell suspension, means for collecting cells in chambers in liquid suspension, and means to store fixed cells for later recovery and examination;[[.]]

means for delivering medium and circulating medium to and from said reactor vessel to form a closed loop;

means for rotating said second rotatable collector plate;

means for exchanging gases between said medium and ambient gas environments;

a computer ~~program~~ with graphical user interface for automatically and/or robotically controlling said reactor vessel;

~~a video camera or video device and microscope~~ an observation system wherein said ~~video camera~~ observation system comprises a camera and a dual optical path configuration allowing for an observation of said cell growth reactor vessel contents and a second microscopic observation path with a 5-micron ~~micron~~ resolution of said cell sample; and

an electrical power source in electrical communication with said means for rotating said reactor vessel, said means for rotating said second collector plate, and said means for delivering and circulating medium.

27. (Canceled)

28. (Currently amended) The bioreactor and cell-culture system according to claim 26, wherein said reactor vessel comprises ~~at least one cylindrical wall and opposing end cover plates and at least on rotary union sealed in fluid communication with said opposing end cover plates~~ and at least two external tubing connectors that articulate said reactor vessel with said closed loop.

29. (Previously presented) The bioreactor and cell-culture system according to claim 28 wherein fluid movement within said closed loop is effected by at least one peristaltic, shuttle or similar pumps that act upon the tubing of the closed loop and do not contact the fluid directly.

30. (Previously presented) The bioreactor and cell-culture system according to claim 29 wherein said fluid movement is controlled by at least one electronically controlled pinch valves that acts upon the tubing of the closed loop and does not contact the fluid directly.

31. (Currently amended) The bioreactor and cell-culture system according to claim 28 wherein said closed-loop bioreactor system is fully enclosed in a first sealed compartment ~~proving~~ providing a level of chemical containment for safely and in which containers used for sample collection are optionally enclosed within a second sealed container within said first sealed container for one additional level of chemical containment and therefore triple chemical containment for safety.

32. (Currently amended) The bioreactor and cell-culturing system according to claim 28 wherein said closed fluid loop includes a plurality of lines providing access for the addition of external fluid to said closed loop and the removal of waste and samples from said closed loop without violating two levels of chemical containment for safety, for making chemical measurements on line, for collecting and fixing cells automatically, for immediate observation by an optionally ~~include~~ included microscope, and for collection in sample containers.

33. (Currently amended) The bioreactor and cell-culture system according to claim 26 further comprising means for measuring pH and dissolved oxygen content of said medium ~~form~~ from said reactor vessel.

34. (Currently amended) The bioreactor and cell-culture system according to claim 26 ~~further comprising a~~ wherein said computer ~~including~~ includes programming for conducting sequences of experimental procedure requiring pumping, valving, chemical measurement, reactor rotating rate, microscope operation without operator intervention or with optional operator intervention.

35. (Previously presented) The bioreactor and cell-culture system according to claim 26 wherein said bioreactor and cell-culture system is capable of functioning in low gravity and that fulfills safety requirements for manned space flight.

36. (Currently amended) The bioreactor and cell-culture system according to claim 26 wherein said second microscopic observation path further comprises ~~comprising~~:

a microscope system for observing suspended cells or organisms within said reactor ~~bioreactor~~ vessel, said microscope system comprising an inlet from a branch of the closed loop coupled to a holder for a hollow microscope slide, a hollow microscope slide made of glass or fabricated by photo polymerization, a light-microscope objective compound lens, a video plane, an outlet for the removal of samples of fluid after observation, and reservoirs for the addition of reagents to cell suspensions when said reagents are required for observation.

37. (Currently amended) The bioreactor and cell culture system of claim 5, further including means for oxygenation of medium in said cell growth reactor vessel comprises passing filtered medium through thin-walled silicone tubing in an oxygen rich environment.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys J. Corcoran can be reached on 571-272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

William H. Beisner
Primary Examiner
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WHB